... *....

(ji **.

į, Ü

Œ

U IJ



- 2. (Amended) A purified pertide according to claim 1 wherein the peptide comprises at least 10 consecutive amino acids of an amino acid sequence selected from the group consisting of [Seq. I.D. Nos.] SEQ ID NOS: 1 and 9.
- 3. (Amended) A purified peptide according to claim 1 wherein the peptide comprises the amino acid sequence shown in [Seq. I.D. No.] SEQ ID NO: 1.
- 4. (Amended) A purified peptide according to claim 1 wherein the peptide comprises the amino acid sequence shown in [Seq. I.D. No.] SEQ ID NO: 4.
- 5. (Amended) A purified pentide according to claim 1 wherein the pentide comprises the amino acid sequence shown in [Seq. I.D| No.] SEQ ID NO: 9.
- 6. (Amended) A specific binding agent that specifically binds to the [a] peptide [having an amino acid sequence selected from the group consisting of Seq. I.D. Nos. 1, 4 and 9] of claim 1.
- 7. (Reiterated) A specific binding agent according to claim 6 wherein the specific binding agent is selected from the group consisting of polyclonal antibodies, monoclonal antibodies and immunologically active fragments of monoclonal antibodies.
- 8. (Reiterated) A specific binding agent according to claim 6 wherein the specific binding agent is conjugated with a detectable label.
- 9. (Reiterated) A method of quantifying the level of expression of a 15 kDa selenoprotein in a biological sample, the method comprising contacting the sample with a specific binding agent according to claim 6 under conditions whereby the specific binding agent forms a complex with any 15 kDa selenoprotein present, and quantifying said complexes.
- 10. (Reiterated) A method of detecting the presence of a 15 kDa selenoprotein in a biological sample, the method comprising contacting the sample with a specific binding agent according to claim 6 under conditions whereby the specific binding agent forms a complex with any 15 kDa selenoprotein present, and detecting the presence of said complex.
- 11. (Reiterated) A kit for detecting or quantifying a 15 kDa selenoprotein, the kit comprising a container containing a specific binding agent according to claim 6.

- 12. (Amended) An isolated nucleic acid molecule that encodes [a polypeptide comprising an amino acid sequence as set forth in Seq. I.D. Nos. 1, 4 or 9] the peptide of claim 1.
- 13. (Amended) [An] the isolated nucleic acid molecule of claim 12, wherein the nucleic acid comprises a [comprising a nucleic acid] sequence selected from the sequences shown in the group consisting of [Seq. I.D. Nos.] SEQ ID NOS: 2, 3 and 8.
- 14. (Reiterated) A recombinant nucleic acid vector including a nucleic acid sequence according to claim 13.
- 15. (Reiterated) A transgenic cell produced by introducing into a cell a vector according to claim 14.
- 16. (Reiterated) A method of generating the purified peptide encoded by the nucleic acid vector of claim 14 by introducing the vector into a cell and expressing the peptide from the cell.
- 17. (Amended) The purified peptide of claim 16 wherein the peptide has an amino acid sequence selected from the sequences shown in the group consisting of [Seq. I.D. Nos.] <u>SEQ ID</u> NOS: 1 and 9.
- 18. (Amended) A purified mammalian 15 kDa selenoprotein having at least 70% sequence identity to SEQ ID NOS: 4, or 9.
- 19. (Amended) A method of detecting the presence of a nucleic acid molecule that encodes [a 15 kDa selenoprotein] the mammalian 15 kDa selenoprotein of claim 18 in a biological sample, comprising:
- (a) contacting the sample with an oligonucleotide comprising at least 15 consecutive nucleotides of a sequence selected from the group consisting of [Seq. I.D. Nos.] <u>SEQ ID NOS:</u> 2 and 8 under conditions whereby said oligonucleotide will specifically hybridize to any nucleic acid molecule present in the sample that encodes [a 15 kDa selenoprotein] the mammalian 15 kDa selenoprotein of claim 18; and
 - (b) detecting the presence of such hybridization.
- 20. (Reiterated) A nucleic acid probe specifically hybridizable to a human 15 kDa selenoprotein RNA or cDNA.

- 21. (Amended) A method of detecting a polymorphism in a human 15 kDa selenoprotein gene, comprising determining all or part of a nucleic acid sequence of [a] the human 15 kDa selenoprotein gene, cDNA or mRNA in a biological sample.
 - 22. (Reiterated) The method of claim 21 wherein the polymorphism is C811/G1125.
- 23. (Reiterated) A method of detecting a polymorphism in a human 15 kDa selenoprotein gene, cDNA or RNA in a biological sample, comprising hybridizing the sample with a nucleic racid probe under conditions whereby the probe will hybridize to the 15 kDa selenoprotein gene, or to cDNA or RNA carrying a polymorphism selected from the group consisting of C811, G1125 and C811/G1125, but not to a wild-type 15 kDa selenoprotein gene, cDNA or RNA.
- 24. (Amended) A method of detecting the mammalian 15 kDa selenoprotein of claim 18 [a 15 kDa selenoprotein] in a cell, comprising administering to the cell ⁷⁵Se, and detecting ⁷⁵Se incorporated into a 15 kDa selenoprotein.
- 25. (Amended) A method for dietary regulation, comprising detecting an abnormally low expression of the mammalian 15 kDa selenoprotein of claim 18 [a 15 kDa selenoprotein] in [the cells] a cell of a mammal and, if the level is [below normal] reduced by at least 3-fold, enhancing the level by providing additional selenium in the diet of the mammal.
- 26. (Amended) The method of claim 25 wherein the detection of [a 15 kDa selenoprotein] the mammalian 15 kDa selenoprotein of claim 18 in the [cells] cell of [a] the mammal is determined by a method selected from the group consisting of Western blotting of the [15 kDa selenoprotein] mammalian 15 kDa selenoprotein of claim 18, Northern blotting of an mRNA coding for the mammalian 15 kDa selenoprotein of claim 18, and Southern blotting of a DNA encoding for the mammalian 15 kDa selenoprotein of claim 18.

Please cancel claims 27 and 28.

29. (Amended) A method for dietary regulation, comprising detecting a [normal] control level of [a 15 kDa selenoprotein] the mammalian 15 kDa selenoprotein of claim 18 in [the cells] a cell of a mammal, determining if the mammal is at an increased risk for cancers associated with defects in the [15 kDa selenoprotein] mammalian 15 kDa selenoprotein of claim 18 and, if the

risk is increased, decreasing the mammal's risk by providing additional selenium in the [diet of the mammal] mammal's diet.

30. (Amended) A method of determining <u>a subject's susceptibility to developing cancer</u> by determining a genotype of a mammalian 15 kDa selenoprotein gene in a sample <u>from the subject</u> comprising:

isolating DNA, cDNA, or man NA from the sample;

amplifying the DNA, cDNA, or mRNA in a region containing a polymorphism at nucleotide positions 811 and 1125;

digesting the amplified DNA eDNA or mRNA with restriction enzyme(s) which can distinguish the polymorphism by a differential restriction fragment length; and detecting the polymorphism by the presence of the differential fragment length.

- 31. (Reiterated) The method of claim 30 wherein the sample comprises a tumor cell.
- 32. (Reiterated) The method of claim 30 wherein the sample comprises a normal cell.
- 33. (Amended) The method of claim 30 wherein detecting the polymorphism comprises amplifying a DNA or cDNA of a mammalian 15 kDa selenoprotein gene with an amplification reaction using primers shown in [Seq. I.D. Nos.] SEQ ID NOS: 12 and 13.
- 34. (Amended) An oligonucleotide comprising a sequence selected from the group consisting of [shown in Seq. I.D. No. 18EQ ID NOS: 12 and 13.

Please cancel claim 35.

- 36. (Amended) A method of determining a sequence of a polymorphism at positions 811 and 1125 of a mammalian 15 kDa selenoprotein gene by using the oligonucleotides of [claims 30 and 31] claim 34 to amplify a region containing the polymorphism.
- 37. (Amended) A transgenic more which overexpresses [an] the isolated nucleic acid molecule of claim 12 [comprising a nucleic acid/sequence selected from the sequences shown in the group consisting of Seq. I.D. Nos. 2, 3, and 8].
- 38. (Amended) A transgenic mouse in which [a] the nucleic acid molecule of claim 12 [comprising a nucleic acid sequence selected from the sequences shown in the group consisting of Seq. I.D. Nos. 2, 3, and 8,] is functionally deleted.



£

W.

T

**.[

Ţ.

- 40. (Amended) The method of claim 39 wherein the protein is expressed by administering the recombinant nucleic acid vector of claim 14 into a subject with an increased predetermined genetic susceptibility to cancer associated with a polymorphism in a 15 kDa selenoprotein gene having at least 70% sequence identity to SEQ ID NOS: 2, 3, or 8, wherein expression of the recombinant nucleic acid in the subject provides a therapeutically effective amount of a 15 kDa selenoprotein having at least 70% sequence identity to SEQ ID NOS: 1, 4 or 9 to the subject.
- 41. (Reiterated) A composition comprising a therapeutically effective amount of the protein of claim 18 and a pharmaceutically acceptable carrier.

Please add the following claims:

- --42. (New) The nucleic acid of claim 13, wherein the nucleic acid sequence has at least 70% sequence identity to SEQ ID NOS: 2, 3 or 8.
- 43. (New) The nucleic acid of claim 13, wherein the nucleic acid sequence has at least 95% sequence identity to SEQ ID NOS 2, 3 or 8.
- 44. (New) The method of detecting a polymorphism of claim 21, wherein the nucleic acid sequence of the human 15 kDa selenoprotein gene has at least 70% sequence identity to SEQ ID NOS: 2, 3 or 8.
- 45. (New) The method of detecting a polymorphism of claim 21, wherein the human 15 kDa selenoprotein gene has the nucleic acid sequence shown in SEQ ID NOS: 2, 3 or 8.
- 46. (New) A method of determining if a subject has an increased risk of developing cancers, comprising determining if there is a polymorphism in the subject's 15 kDa selenoprotein gene.

al.

- 47. (New) The method of claim 48, wherein the 15 kDa selenoprotein gene has at least 70% sequence identity to SEQ ID NO\$: 2, 3 or 8.
- 48. (New) The method of claim 48, wherein the polymorphism is selected from the group consisting of C811, G1125 and C811/G1125.
- 49. (New) The method of claim 21, wherein detecting a polymorphism in a human 15 kDa selenoprotein gene is used to determine if a human has an increased risk of developing cancers.
- 50. (New) The method of claim 23, wherein detecting a polymorphism in a human 15 kDa selenoprotein gene is used to determine if a human has an increased risk of developing cancers.
- 51. (New) A method of determining if a subject has an increased risk of developing cancers, comprising determining if the subject has an abnormally low expression of the purified mammalian 15 kDa selenoprotein of claim 18 in the cells of the subject.
- 52. (New) The method of claim 51, wherein the expression of the purified mammalian 15 kDa selenoprotein of claim 18 is reduced by at least 3-fold.
- 53. (New) The method of claim 51, wherein the expression of the purified mammalian 15 kDa selenoprotein of claim 18 is reduced by at least 50%.
- 54. (New) A method for dietary regulation, comprising detecting an abnormally low expression level of the purified mammalian 15 kDa selenoprotein of claim 18 in a cell of a mammal and, if the level is reduced by at least 50%, enhancing the level by providing additional selenium in the diet of the mammal.
- 55. (New) The method of claim 25 wherein the mammalian 15 kDa selenoprotein of claim 18 has at least 95% sequence identity to SEQ ID NOS: 1, 4, or 9.
- 56. (New) The method of claim 30, wherein the mammalian 15 kDa selenoprotein gene has at least 70% sequence identity to SEOID NOS: 2, 3 or 8.
- 57. (New) The method of claim 36, wherein the mammalian 15 kDa selenoprotein gene has at least 70% sequence identity to SEQ ID NOS: 2, 3 or 8.